

In the Claims

1. - 92. (Cancelled)

93. (New) A detection method for intracellular integrase activity of an integrase protein encoded by an integrase gene using a promoterless reporter gene construct.

94. (New) The detection method of claim 93, wherein the integrase activity is present in cell culture or as a result of transfection of an integrase gene, said integrase activity being performed by a wild type or a mutated integrase gene.

95. (New) The method according to claim 93, wherein the integrase gene is mutated in order to obtain an optimised codon usage by

- a) Choosing alternative codons in favour of preferred codons found in strongly expressed human genes,
- b) Choosing alternative codons such as to have a GC nucleotide pair frequency within the range between 53 and 63%.

96. (New) The method according to claim 93, wherein the integrase gene is mutated in order to obtain an optimised codon usage by

- a) choosing alternative codons in favour of preferred codons found in strongly expressed human genes,
- b) Choosing alternative codons such as to have a GC nucleotide pair frequency within the range between 53 and 63%,

and wherein said integrase gene is further redesigned based on one or more of the following principles:

- (i) removal of potential splice sites
- (ii) reduction of CpG methylation sites
- (iii) introduction of 5' and 3' untranslated regions
- (iv) addition of an extra N-terminal peptide

97. (New) The method according to claim 93, wherein the integrase protein encoded by an integrase gene is selected from the class of a retroviral a lentiviral or an HIV integrase.
98. (New) The method according any to claim 93, wherein the promoterless reporter gene is one of a luciferase, GFP, antibiotic selection marker and a cytotoxic drug resistance gene.
99. (New) The method according to claim 93, wherein the promoterless reporter gene construct is generated from the reporter gene and the construct is used as the substrate of an enzymatically active retroviral protein expressed from a synthetic gene, or wherein a reporter gene construct is generated from the reporter gene and the construct contains an internal IRES, or wherein the reporter gene codes for an enzyme.
100. (New) The method according to claim 93, wherein said integrase protein is encoded by a synthetic retroviral pol gene or a region of a retroviral pol gene the retroviral gene having non-preferred codons when referred to the eukaryotic cell, the number of non-preferred codons being such that replacement of all the non-preferred codons by preferred codons for the eukaryotic cell results in a GC dinucleotide pair content of 65 % or higher, the synthetic gene having a nucleotide pair content between 53 and 63 %, more preferably between 55 and 61 % and the expressed retroviral protein is expressed at a level to provide detectable enzymatic activity of the expressed retroviral protein in the eukaryotic cell.
101. (New) The method according to claim 93, wherein the detection of integrase activity includes at least promotion or stimulation of integration of DNA fragments into the host cell DNA, preferably the chromosome of the host cell.
102. (New) The method according to 93, wherein said integrase protein has an expression level of at least 200% of that expressed by a wild type integrase protein in a eukaryotic cell.

103. (New) The method according to claim 93, wherein the integrase gene is a synthetic gene which comprises the sequence of Fig2A or homologs thereof which have a GC content between 53 and 63 %, preferably between 55 and 61 %.

104. (New) Use of a method according to claim 93 for screening for integrase inhibitors.

